

*cn+*  
*a*  
*1*

albumin (BSA) for 5 days. The area in the vicinity of the beads shows normal structures with thin ectodermal (ec) and endodermal (en) epithelia enclosing the mesodermal (me) stroma. The original positions of some gel beads (g) are distinguishable by indentations in the ectodermal surface of the CAM. The mesoderm consists primarily of sparse and loosely arranged fibroblasts in wide intercellular spaces. Occasional large blood vessels (bv) with nucleated erythrocytes are observed in the mesoderm. The ectoderm exhibits normal development of the intradermal capillaries (iec). Stained collagen fibers are sparsely distributed in some regions within the mesoderm. Vestiges of gelatin (gl) remain between the beads and in the regions between the beads and the stratified ectoderm. Scale bar = 50  $\mu\text{m}$ .

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In the BRIEF DESCRIPTION OF THE DRAWINGS, please substitute the description of figure 4 on page 9, lines 11-24 with the following:

*a*  
*2*

**Figure 4.** Histological response of chick chorioallantoic membrane (CAM) after the application of 20 ng pTGF- $\beta$ 1. There is a distinct thickening of the mesoderm (me) and extensive stratification of the endoderm (en). A widespread proliferation of capillaries (ca) is observed throughout the mesoderm. A discrete accumulation and condensation of the fibrous connective tissue (ct), which is mainly localized in the endodermal portion of the mesoderm, accompanies the increase in the number of capillaries. Stained collagen fibers

*chart  
A 2*

are densely spread in the condensed fibrous tissue within the mesoderm in the locality of the reaction center. Sloughing of the endodermal cells (arrowhead) is observed.  
Scale bar = 100  $\mu\text{m}$ .

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In the BRIEF DESCRIPTION OF THE DRAWINGS, please substitute the description of figure 5 spanning pages 9-10 with the following:

*A 3*

**Figure 5.** Histological response of chick chorioallantoic membrane (CAM) after exposure to 500 ng of bFGF. There is a distinct thickening of the mesoderm (me) and extensive stratification of both the ectoderm (ec) and endoderm (en). Dense accumulations of fibroblast-rich connective tissue (ct) are localized in areas close to both the ectodermal and the endodermal portions of the mesoderm. Capillaries (ca), as well as a large number of blue-staining collagen fibers, are spread widely throughout the reactive mesoderm. Clusters of cells (cd) with a similar appearance to the stratified ectoderm are embedded within the mesoderm. Stained collagen fibers are densely spread in the condensed fibrous tissue within the mesoderm in the locality of the reaction centers and finely spread in the central portion of the mesoderm. Remnants of gelatin (gl) are located between the beads and in the vicinity of the ectoderm.  
Scale bar = 100  $\mu\text{m}$ .

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In the BRIEF DESCRIPTION OF THE DRAWINGS, please substitute the description of figure 7 on page 11, lines 6-16 with the following:

*A4*

**Figure 7.** Histological reaction of a chick chorioallantoic membrane (CAM) after the application of a combination of hOP-1/bFGF (100/100 ng). Numerous distended blood vessels (bv) and capillaries (ca) with nucleated erythrocytes are widely distributed within the oedematous mesoderm (me). The fibrous connective tissue (ct), consisting of stained collagen fibers, is very dense and widely distributed throughout the thickness of the reactive mesoderm. The endoderm (en) and the ectoderm (ec) (not in this section) thickened by stratification. Scale bar = 50  $\mu\text{m}$ .

In the BRIEF DESCRIPTION OF THE DRAWINGS, please substitute the description of figure 8 spanning pages 11-12 as follows:

*A5*

**Figure 8.** Chick chorioallantoic membrane (CAM) response following exposure to hOP-1/pTGF- $\beta$ 1. (A) hOP-1/pTGF- $\beta$ 1 (100/5 ng): there is a very marked thickening of all the three layers of the CAM. The multilayered endoderm (en) exhibits a villi-like pattern. Widespread capillaries (ca) and fibrous tissue (ct) are located over the entire reactive mesoderm (me) containing numerous distended blood vessels (bv). Stained collagen fibers are densely spread in the condensed fibrous tissue within the mesoderm in the locality of the areas adjacent to the ecto- and endoderm and finely spread in the central portion of the mesoderm. Clusters of cells (cd) with a similar appearance to the stratified ectoderm are embedded within the mesoderm. Sloughing of the endoderm (arrowheads) is clearly visible.

*cn't*  
*as*

Scale bar = 50  $\mu\text{m}$ . (B) hOP-1/pTGF- $\beta$ 1 (100/20 ng): There is extensive fibrous tissue (ct) condensation and prominently high number of capillaries (ca). Evidence of bead (g) encapsulation is clearly noticeable. The dense connective tissue fibers including the blue-staining collagen, are aligned in the region skirting the zone of encapsulated beads. The multilayered endoderm (en) is villi-like and the thickened ectoderm is vessel-free. Sloughing of the endoderm (arrowhead) is clearly visible. Scale bar = 100  $\mu\text{m}$ .

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On page 42, please replace the first full paragraph on lines 11-20 with the following:

*a*  
The amino acid sequences of COP5 (SEQ ID NO:11) and COP7 (SEQ ID NO:12) are shown below, as set forth in Oppermann et al., U. S. Patent Nos. 5,011,691 and 5,324,819, which are incorporated herein by reference:

COP5 LYVDFS-DVGW**D**DWIVAPPGY**Q**AFYCHGECPFPLAD

COP7 LYVDFS-DVGW**N**DWIVAPPGY**H**AFYCHGECPFPLAD

COP5 **H****F**NSTN--H-AVVQTLVNSVNSKI--PKACCVPTELSA

COP7 **H****L**NSTN--H-AVVQTLVNSVNSKI--PKACCVPTELSA

COP5 ISMLYLDENEKVVLKYNQEMVVEGCGCR

COP7 ISMLYLDENEKVVLKYNQEMVVEGCGCR

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Applicants describe the specific amendments to the specification using the bracket and underline format in the "Appendix of Specification Amendments" enclosed as Tab A, which is attached hereto.